Diagnosis of Obstructive Jaundice in Infants: Tc-99m DISIDA in Duodenal Juice

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Technetium-99m di-isopropylphenylcarbamoylmethylimidodiacetic acid cholescintigraphy, together with measurements of radioactivity in duodenal juice, was used to evaluate 23 infants with prolonged obstructive jaundice. Four patients proved to have biliary atresia. The remainder had neonatal hepatitis. There was distinct differentiation of biliary atresia from neonatal hepatitis when the time-activity curves were analyzed. In neonatal hepatitis the radioactivity in duodenal juice is obviously higher, peaking above 1500 cpm/100 μl per mCi dose. In biliary atresia the pattern is flattened, with maximal activity below 500 cpm/100 μl per mCi dose.

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Neonates with prolonged obstructive jaundice pose a diagnostic problem that may remain unsolved by routine clinical and laboratory examinations, especially in the commonly encountered neonatal hepatitis and biliary atresia. Reliable discrimination between these two entities is of great clinical importance. Infants with biliary atresia must be operated on as early as possible to avoid an otherwise fatal outcome (*1–3*). On the other hand, neonatal hepatitis is a self-limited disease, and laparotomy would increase morbidity and mortality (*4,5*). Technetium-99m cholescintigraphy was thought to be the most sensitive way to separate these two entities, (*6–10*) but the specificity is not fully satisfactory. In the present study we attempted to establish a more reliable method by analyzing the radioactivity in duodenal juice in conjunction with di-isopropylphenylcarbamoylmethylimidodiacetic acid (Tc-99m DISIDA) cholescintigraphy.

MATERIALS AND METHODS

Twenty-three infants with prolonged obstructive jaundice were studied prospectively. The patients ranged in age from 40 to 105 days. The sex, serum bilirubin levels, and final diagnoses are summarized in Table 1. The diagnoses were individually confirmed by laparotomy, liver biopsy, and/or by following the clinical course.

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All patients had their initial examinations after oral phenoborbital therapy (5 mg/kg-day) for at least 3 days (3–15 days). The infants were given nothing by mouth for 3 hr before the examination. Fluid was supplied intravenously. A radiopaque infant-size duodenal tube was positioned between the second and third portions of the duodenum, as confirmed by brief fluoroscopy. Duodenal juice was collected by aspiration through the duodenal tube. One millicurie of Tc-99m DISIDA was given intravenously after the initial collection of duodenal juice. Then 1 to 2 ml of duodenal juice was collected at 5, 15, 30, and 45 min after injection, and at 1, 2, 3, and 4 hr. After adequate mixing, paired samples of 100 μl of duodenal juice were obtained from each collection. All samples were counted by gamma counter at 5 hr after injection. We recorded the average values of compatible paired data, sampling again if they were not compatible. The results were plotted into a time-activity curve for each patient.

Sequential anterior scintigrams of the abdomen were also obtained 1, 5, 15, and 30 min after injection, and at 1, 2, and 4 hr. Delayed images were obtained at 24 hr if there were still nonvisualization of gallbladder or bowel activity by 4 hr.

RESULTS

Nineteen patients finally proved to have neonatal hepatitis, and four had biliary atresia. In the group of neonatal hepatitis, the images showed the gallbladder activity in only three cases, bowel activity in only eight

TABLE 1. CLINICAL AND LABORATORY DATA IN 23 INFANTS WITH PROLONGED OBSTRUCTIVE JAUNDICE

Patient No.	Sex	Exam No.	Age (days)	Bilirubin (mg/dl) total/direct	Image findings: Gallbladder visualized	Image findings: Tracer in bowel	Bile-stained in duodenal juice	Maximal radioactivity in 100 μl of duodenal juice (cpm/mCi)	Final diagnosis
1	F	1	40	13.2/8.4	−	−	−	427	Biliary atresia
2	F	1	72	15.1/9.5	−	−	−	173	Biliary atresia
3	M	1	85	8.2/5.5	−	−	−	474	Biliary atresia
		2	91	8.8/6.5	−	−	−	484	
4	M	1	105	9.8/3.9	−	−	−	151	Biliary atresia
5	F	1	84	8.3/6.1	+	+	+	27,468	Neonatal hepatitis
6	M	1	69	4.8/3.2	+	+	+	46,484	Neonatal hepatitis
7	M	1	42	5.6/3.8	+	+	+	83,311	Neonatal hepatitis
8	M	1	45	8.4/5.2	+	+	+	2,204	Neonatal hepatitis
9	M	1	58	8.7/5.9	−	+	+	67,865	Neonatal hepatitis
10	M	1	41	9.5/6.5	−	+	+	111,004	Neonatal hepatitis
11	M	1	59	4.8/3.7	−	+	+	2,228	Neonatal hepatitis
		2	63				+	22,745	
12	M	1	81	7.5/5.2	−	+	+	53,680	Neonatal hepatitis
13	M	1	44	11.2/7.3	+	−	+	4,301	Neonatal hepatitis
14	M	1	44	7.1/4.8	+	−	+	12,619	Neonatal hepatitis
15	M	1	58	10.4/6.8	−	+	−	1,639	Neonatal hepatitis
16	M	1	49	19.8/13.6	−	+	−	3,882	Neonatal hepatitis
17	F	1	52	7.9/5.7	−	+	−	2,725	Neonatal hepatitis
18	M	1	75	11.1/8.1	−	+	+	2,197	Neonatal hepatitis
19	M	1	44	4.0/3.1	−	−	+	3,451	Neonatal hepatitis
		2	56	4.0/3.2	+	−	−	2,381	
20	F	1	75	9.2/5.8	−	−	−	2,238	Neonatal hepatitis
		2	84	7.8/5.6	−	−	−	13,956	
21	M	1	49	12.3/7.9	−	−	−	2,138	Neonatal hepatitis
22	M	1	64	5.1/4.0	−	−	−	1,576	Neonatal hepatitis
23	M	1	59	5.8/3.8	−	−	−	1,855	Neonatal hepatitis

cases, and both in four cases. The remaining four cases of neonatal hepatitis showed neither gallbladder nor bowel activity by 24 hr. All of the patients with biliary atresia failed to visualize either gallbladder or bowel activity (Table 1). For the diagnosis of biliary atresia, the sensitivity is 100% but the specificity is only 78.9%. The accuracy is 82.6%, and the positive predictive value is 50%.

None of four cases with biliary atresia had bile stain in the duodenal juice. On the other hand, 12 out of 19 cases of neonatal hepatitis showed bile staining. Based on the appearance of positive or negative bile staining, the sensitivity of diagnosis is 100%, the specificity is 63.2%, the accuracy is 69.6%, and the positive predictive value is 36.4%.

With analysis of the time-activity curves from duodenal juice, cases of neonatal hepatitis had maximal activities varying from 1,576 to 111,040 cpm/100 μl of duodenal juice per mCi dose, whereas cases of biliary atresia had maximal activities varying from 151 to 484 cpm/100 μl-mCi (Table 1). Biliary atresia gave a flattened pattern, but neonatal hepatitis showed obvious rise of activity after 30 min (Fig. 1). The method therefore provides clear discrimination between neonatal hepatitis and biliary atresia.

DISCUSSION

About 75% of cholestasis in neonates fall into the two categories of biliary atresia and neonatal hepatitis (*11*). Although Landing (1974) proposed that neonatal hepatitis and biliary atresia represent different responses to similar perinatal insults, presumably infectious, (*12*) the management and prognosis of neonatal hepatitis and biliary atresia differ. Neonatal hepatitis is a self-limited disease without specific therapy and with a cited mortality of 10% to 40% (*11*). Untreated biliary atresia is bound to be fatal, with 95% of the patients dying before age 2 (*4,11,13*). Portoenterostomy (Kasai procedure) has dramatically improved the survival of infants with

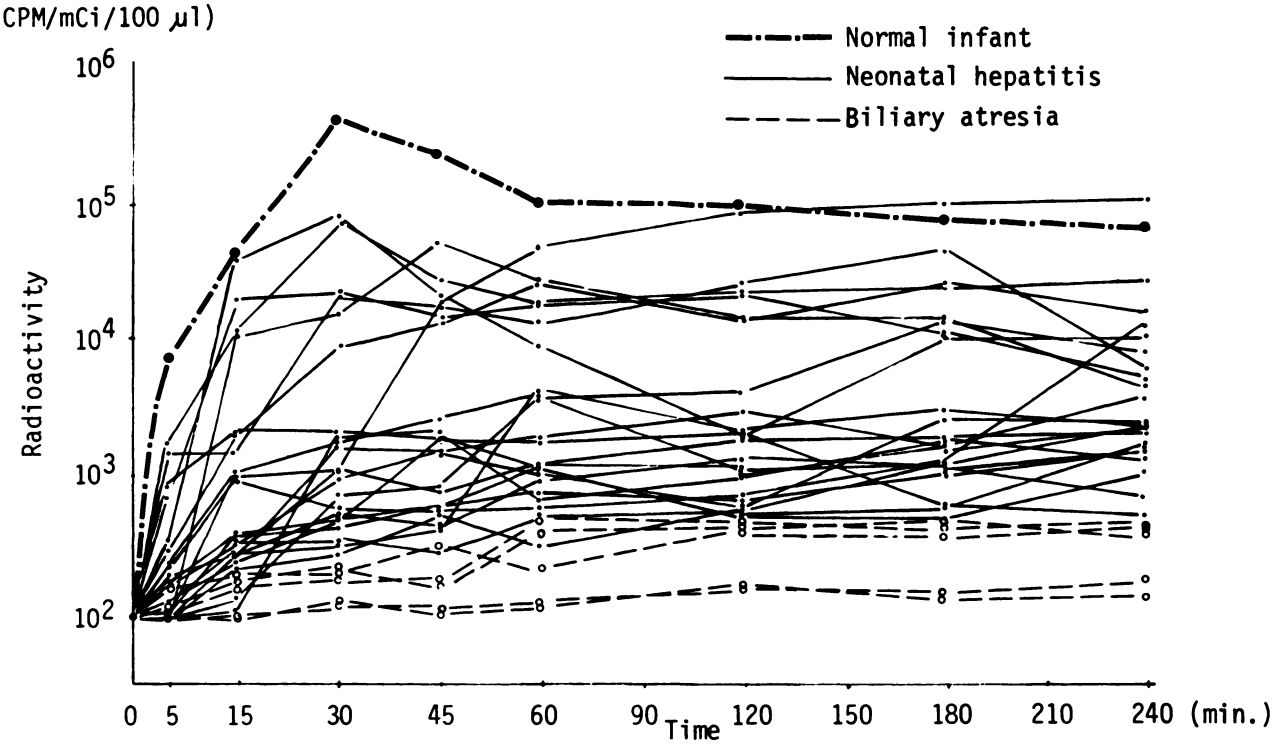

FIG. 1. Time-activity curves of duodenal juice in 23 infants with prolonged obstructive jaundice

biliary atresia, (*14*) and there is now a 30% to 40% 4-yr survival rate (*15*). Kasai et al. report long-term survival of more than 22 yr (*14,16*). The age of the patient at the time of surgery is crucial. Long-term follow-up studies indicate that results are significantly better when surgery is performed before 10 wk of age (*16*). Although laparotomy with operative cholangiography can provide a direct and definite diagnosis, (*17,18*) it increases the risk of cirrhosis and mortality in cases of neonatal hepatitis (*5*). Thus it is very important to differentiate these two entities early and accurately by noninvasive methods.

Routine clinical and laboratory studies pose a diagnostic dilemma. Many tests have been used to evaluate prolonged obstructive jaundice in infants, including clinical scoring, alpha-fetoprotein, lipoprotein-x, serum gamma glutamyl transpeptidase, liver aspiration biopsy, laparoscopy, and fecal excretion of I-131 rose bengal (*19-24*). No single test or combination of tests has proven infallible. Recently Tc-99m cholescintigraphy has been considered the most accurate method of diagnosis (*6-10*). The sensitivity is good, but the specificity varies with the Tc-99m labeled radiopharmaceutical used. Studies in baboons have shown that agents similar to Tc-99m DISIDA are superior hepatobiliary radiopharmaceuticals (*25,26*). Clinical studies in a variety of hepatobiliary diseases have also showed that Tc-99m DISIDA rapidly clears from the blood, yielding satisfactory to excellent images of the biliary system with minimal interference from renal activity (*27,28*). In the present study, the sensitivity is 100% and specificity is 78.9%. Four of our 23 cases could not be differentiated by observation of Tc-99m DISIDA cholescintigrams.

Greene et al. report that accurate differentiation between biliary atresia and neonatal hepatitis can be achieved by observing a 24-hr collection of duodenal juice for the presence of bilirubin staining (*29*). In the present series, however, we failed to detect visible bilirubin staining of the duodenal juice in seven cases of neonatal hepatitis.

Serial measurements of radioactivity in duodenal juice offer a time-activity curve, corresponding to the biliary dynamics. They separate biliary atresia from neonatal hepatitis without difficulty. Biliary atresia yields a flattened time-activity curve with the maximal activity in duodenal juice below 500 cpm/100 μl per mCi of dose. In neonatal hepatitis the activity of duodenal juice increases progressively after administration of Tc-99m DISIDA, and after 30 min it reaches a maximum that is usually higher than 1,500 cpm/100 μl-mCi. There was a clear-cut discrimination between the two entities.

Regarding the insertion of the duodenal tube, we found that the procedure was safe and easily done. The common practice of duodenal feeding in many neonatal units attests to the ease with which duodenal tube placement can be achieved. Gastric insufflation of air and a right decubitus position of the infants greatly aid passage of the tube into the duodenum (*30,31*). The entire procedure usually requires less than 10 min. Although morbidity associated with prolonged use of a polyvinyl feeding tube has been reported, (*32*) we have

observed no major complication of duodenal intubation in the present series as well as elsewhere in our neonatal unit. Sneezing and rhinorrhea due to irritation by the tubes occurred only in some cases, and, these symptoms usually subsided promptly without therapy.

Brief fluoroscopy was performed to document the position of the duodenal tube. It involves the risk of increased radiation dose to the infants, but the duration of exposure can be minimized by other ways of confirming the position of the tube in the duodenum before fluroscopy, such as by determining the pH of the aspirate or by failure to aspirate air (*31*).

It is emphasized, therefore, that serial analysis of radioactivity in the duodenal juice after administration of Tc-99m DISIDA may offer a highly specific and sensitive method for differential diagnosis of biliary atresia from neonatal hepatitis. More cases will be studied to evaluate the accuracy of this examination.

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